Published in final edited form as:

Urology. 2008 December 1; 72(6): 1303–1304. doi:10.1016/j.urology.2008.06.056.

Editorial Comment on adjuvant radiotherapy study

Ian M. Thompson, MD

University of Texas Health Science Center at San Antonio

When asked to write this editorial, I initially demurred. Reasoning: the subject at hand is the subject of two randomized controlled studies of almost 1500 subjects; both have reported initial results. The EORTC trial, a study of about 1,000 men has reported short-term results: a significant reduction in PSA relapse with radiation.¹ SWOG 8794, with longer followup showed an even greater reduction in biochemical failure, delaying median time to failure by 7 years.² However, the primary endpoint for our study – metastasis-free survival – was reduced by 25%, but just missed statistical significance ($p=0.06$). We recently reported updated data at the 2008 AUA meeting.³

What's the point of this editorial? The SWOG and EORTC trials were developed in response to hundreds of case series and reviews on this subject. Some are pro-radiation and some are pro-observation, following PSA, and treating later – either at PSA relapse or for symptoms. Clinicians can find support for either approach, based on which case series they read or opt to cite.

This is not the way to advance medical care; with the completion of phase 3 trials, it is my opinion that reporting of case studies, with their inherent biases (patient selection, uneven followup regimens, differing prompts for adjuvant therapy, non-standardized treatments, lack of quality assurance for treatment and followup, etc), should stop. Readers should examine a single reference.⁴ The authors report how long journals and authors take to stop publishing papers on unproven therapies after the completion of an enormous clinical trial; curiously, publications continued for years after the treatment was debunked.

Sorry folks, but history has demonstrated that when it comes to determining which of two treatments is optimal, little can be learned from case series, no matter how hard the investigators try to control for covariates; there are so many confounds which you cannot control or measure so that your results and comparisons are unreliable. Only through randomized trials can you get an answer. Our plaintive reply is “they’re too hard, they take too long, we can’t do them”. That’s not an excuse; our colleagues in other disciplines expect these challenging studies to be accomplished, do not rely on observational data, and with perseverance, accomplish *difficult trials*.^{5,6} Ultimately, our patients deserve them. Finally, I would encourage journals (and authors) to consider a modest proposal: once phase 3 data are available, think twice about publishing another case series; devote your effort into registering a patient.

References

1. Bolla M, van Poppe HI, Collette L, et al. European Organization for Research and Treatment of Cancer. Postoperative radiotherapy after radical prostatectomy: a randomized controlled trial. *Lancet* 2005;366:572–574. [PubMed: 16099293]
2. Thompson IM, Tangen CM, Paradelo J, Lucia MS, Miller G, Troyer D, Messing E, Forman J, Chin J, Swanson G, Canby-Hagino E, Crawford ED. Adjuvant radiotherapy for pathologically-advanced prostate cancer: Results of a randomized, prospective clinical trial. *JAMA* 2006;296:2329–35. [PubMed: 17105795]
3. See “Take Home Messages” lecture from AUA:
<http://webcasts.prous.com/aua2008/webcaster/template/player.asp?id=336&q=256&v=wm&tgs=&webcast=takehome&CLID=2&CID=YY&CMEID=>
4. Tatsioni A, Bonitsis NG, Ioannidis JPA. Persistence of contradicted claims in the literature. *JAMA* 2007;298:2517–26. [PubMed: 18056905]
5. Hobson RW 2nd, Weiss DG, Fields WS, Goldstone J, Moore WS, Towne JB, Wright CB. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. The Veterans Affairs Cooperative Study Group New England. *Journal of Medicine* 1993;328:221–7.
6. Fisher B, Bauer M, Margoless R, Poisson R, Pilch Y, Redmond C, Fisher E, Wolmark N, Deutsch M, Montague E, et al. Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. *New England Journal of Medicine* 1985;312:665–73. [PubMed: 3883167]